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10/642,615	08/19/2003	Ali Afzali-Ardakani	YOR920030023US1	3761

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EXAMINER	
GAKH, YELENA G	

ART UNIT	PAPER NUMBER
1797	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/642,615	AFZALI-ARDAKANI ET AL.	
	Examiner	Art Unit	
	Yelena G. Gakh, Ph.D.	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/09/07*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 10-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 10-18* is/are rejected.

7)☒ Claim(s) *10* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Amendment filed on 11/09/07 is acknowledged. Claims 1-4 and 10-18 are pending in the application. The examiner repeats the description of her approach to examining the instant application from the previous Office action:

The examiner considers the subject matter of the pending claims in two ways - first, as the recitation of the molecular manipulator as disclosed in the specification, i.e. the molecule, which is capable of acting as tweezers because of changes in its steric structure; and second, as the recitation of the light-sensitive molecule attached to the probe, irrelevant of its function. As demonstrated by the examiner below, the claims considered in the first way are rejected as not being enabled by the specification, since the specification does not enable using the molecules recited in the claims as molecular manipulators, not mentioning the hypothetical nature of the molecules. The claims considered in the second way are rejected over the prior art, since the prior art discloses light-sensitive molecules, specifically azo-molecules undergoing cis-trans isomerism under UV radiation, attached to the probe.

Response to Amendment

2. In response to the amendment the examiner modifies rejection of the claims over the prior art and under 35 U.S.C. 112, first and second paragraphs. Objection to the specification is sustained.

Specification

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to as not enabling the use of the hypothetical molecules disclosed in the specification as the molecular manipulator. The disclosure describes in general terms the Applicants' hypothesis for a possible molecular manipulator, without any evidence for enabling the Applicants' hypothetical molecule. The molecules depicted on Figures 1 and 2 are

not CA registered (the library search report is attached) and obviously do not exist. The Applicants did not provide any possible synthetic path for obtaining such molecules, not mentioning their testing as molecular manipulators. The hypothesis is not experimentally proven. The structure indicated as an example cannot be used as a manipulator as disclosed in the specification, since it would have a highly non-planar structure, contrary to what is depicted in the drawings. Moreover, its steric configuration and energetic state would not provide conditions favorable for using such molecules as manipulators as can be clearly seen from the prior art described below, which is especially true for the prophetic example depicted on Figure 2..

A. Rejection of the pending claims read in light of the specification.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-4 and 10-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The Breath of the Claims

The claims recite in the most general terms "a molecule manipulator" comprising a light-sensitive molecule with two azo double bonds which change their configuration upon light irradiation, with the molecule attached to the probe of a scanned-proximity probe microscope. No specifically synthesized molecules, which can act as molecular manipulators as recited in the claims, are disclosed in the specification. The example depicted on Figure 2 is not a real molecule and is not enabled as the molecular manipulator. The specification does not provide

any guidance for synthesis of such molecule or any evidence of its ability to act as a molecular manipulator.

The Nature of the Invention

The invention is directed toward a hypothetical molecular manipulator based on a known fact of *cis-trans* light-induced transformation of azo-bond. The only prophetic example for the claimed "manipulator" is depicted on Figure 2. The Applicants drew only *trans*-form of the manipulator, as it would be clear from the drawing of *cis*-form that the form is totally unrealistic because of the severe steric hindrance, which would be created between two proximate arms. Since the arms can relatively freely rotate about Ph-Ph bonds, the configuration with the two arms turned to each other would be avoided, even if such molecule could be synthesized.

The State of the Prior Art

The state of the prior art has been described in details in previous Office actions. All references teaching molecular manipulators and tweezers describe extensive research of rigid structures with specific and well defined geometrical parameters, as well as entropy calculations. None of the recited papers indicate the possibility of using molecules recited in the claims and depicted on Figure 2 as molecular manipulators, because of unrealistic nature of these molecules and their existence in *cis*-form, which would be a necessary condition for the molecules to be used as molecular manipulators.

The Level of One of Ordinary Skill

There is no way for any person of an ordinary skill in the art to obtain *cis*-form of the molecule depicted in Figure 2 as a prophetic example of the molecules recited in the claims, since proximity of two bulky arms in their *cis*-configurations would create a severe steric hindrance, which could be easily avoided by rotation of the arms about single Ph-Ph bonds, with the rotation totally preventing the molecule to be used as a molecular manipulator or tweezers.

The Level of Predictability in the Art

The prior art does not provide a ground for any expectation of success for using such structures as the one depicted on Figure 2, as molecular manipulators. Not only the disclosed manipulators do not have well defined rigid structures with parameters that fit sizes of potential analytes to be manipulated, - the requirement well established by the prior art, - but also the structure depicted on Figure 2 can hardly exist in *cis*-configuration as indicated above.

The Amount of Direction Provided by the Inventor

The instant disclosure does not provide any direction to the synthesis of the hypothetical structures disclosed in the specification, or to their application as molecular manipulator. The specification does not provide any guidance for transferring *trans*-form depicted on Figure 2 into *cis*-form and for using it as a molecular manipulator, nor does it indicate, as to how such *cis*-form can exist.

The Existence of Working Examples

No working examples are provided by the specification for either the synthesis of the compounds disclosed in the specification and their attachment to the microscope probe, or for their application as molecular manipulators. The Applicants did not provide any evidence for the possibility of the structure depicted on Figure 2 to exist in *cis*-form.

The Quantity of Experimentation Needed
to Make or Use the Invention Based on the Content of the Disclosure

It would require an undue experimentation for a routineer in the art to synthesize hypothetical compounds disclosed in the specification; it would require even more of undue experimentation to study them as potential molecular manipulators with a very little expectation for success, since the structures do not meet any requirements established by the prior art for the molecular manipulators. Moreover, it seems to be quite improbable for a routineer in the art to obtain any structure similar to the one depicted on Figure 2 as a prophetic example of the claimed molecular manipulators, because the structure can hardly exist in *cis*-form.

B. Rejection of the pending claims as reciting molecules attached to the probe unrelated to their intended use disclosed in the specification.

Claim Objections

6. Claim 10 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Any azo double bond undergoes *cis-trans* isomerization upon irradiation with UV light, and therefore the recitation of claim 10 does not further limit the subject matter of the parent claim, since both azo groups will undergo the same isomerization.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-4, 10-16 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites "a moiety located between the two arms". It is not clear, what this moiety that is "located" between the two arms might be. Is this the central part of the molecule between two arms? Then why is it "located" there, when this is a fragment of the same molecule, to which two arms belong? Since the molecule is supposed to work as molecular tweezers, the claim can be interpreted as reciting the light-sensitive molecule holding the chemical moiety between its arms. The language renders claim 1 and all dependent claims indefinite, since no definition for a "moiety located between the two arms", with the arms disclosed as being able to hold another molecule, is provided in the specification. The specification does not disclose, whether the moiety is another molecule located between two arms, or it is a central part of the same molecule.

From claim 2 it is not clear, what is "a line" of a scanned-proximity probe microscope, and how can the light-sensitive molecule be attached to the line?

Claim Rejections - 35 USC § 103

9. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

10. **Claim 1-4, 10-16 and 18** is rejected under 35 U.S.C. 103(a) as being unpatentable over Stiller et al. (Surface and Interface Analysis, 2000) in view of Seves et al. (J. Appl. Polym. Sci., 1991) (Seves).

In their paper Stiller et al. (Stiller) disclose "scanning Kelvin microscopy as a tool for visualization of optically induced molecular switching in azobenzene self assembling films" (Title). The light-sensitive azo-benzene derivative comprises two arms, one of which includes the double bond –N=N–, which undergoes cis-trans isomerization upon illuminating with UV light, and the other one is different from –N=N– - bond (Figure 1), attached to the scanning force microscopy (SFM) probe, which conventionally comprises any of silicon, silicon oxide, aluminum oxide or titanium oxide (claims 1-7). Since the moiety recited in the claims does not have a definite and clear interpretation and can be interpreted in various ways, the examiner considers the phenyl ring to be such moiety (claim 11). The functional group R is CF_3 (a haloalkyl) (claim 12). The molecule is covalently bound to the probe through SH-group (claims 13-14). The probe is coated with gold (claim 16). The arms have different lengths (claim 18) and a space between them (the whole molecular fragment between them).

Stiller does not specifically disclose a light-sensitive azo-derivative with two arms, each having the azo double bond.

Seves teaches "thermal cis-trans isomerization of azo dye chrysophenine in cellulose matrices" (Title), with the dye being a molecule with two arms each comprising azo double bond and a central part (a moiety?) in between.

It would have been obvious for any person of ordinary skill in the art to utilize chrysophenine comprising two arms each having azo double bond, which is recited by Seves, for visualization of optically induced molecular switching in azobenzene, with a routine derivatization of one of the functional groups of the molecule to attach it to the SFM probe, as taught by Stiller, in order to analyze enhanced effect of two azo bonds undergoing *cis-trans*

izomerization. Furthermore, the instant specification discloses two arms with one or two azo-bonds in the arms as obvious modifications (see page 12).

11. **Claim 17** is rejected under 35 U.S.C. 103(a) as being unpatentable over Stiller in view of Seves, as applied to claims 1-4, 10-16 and 18 above, and further in view of the prior art disclosed by Nakagawa (US 5,353,632).

While Stiller in view of Steves do not specifically disclose coating comprising trichlorosilane, Nakagawa describes such coating as being conventional and disclosed in the prior art: "the other insulation comprises octadecyl-trichlorosilane (OTS)" (see Background of the Invention, col. 1, line 56). Therefore, it would have been obvious for any person of ordinary skill in then art to apply OTS coating indicated by Nakagawa to the probe disclosed by Stiller modified by Seves as an additional protection layer with an obvious modification of the moiety of the azo-compound to covalently bind to the coating, which would be within the skill of a routineer in the art.

Response to Arguments

12. Applicant's arguments filed 11/09/07 have been fully considered but they are not persuasive.

Regarding rejection of the pending claims under 35 U.S.C. 112, first paragraph, the Notice of Panel Decision from Pre-Appeal Brief Reviews indicates that the rejection is withdrawn for *re-opening* the prosecution, not that the rejection is withdrawn *per se*. The examiner re-opened the prosecution with establishing the two-way rejection, as clearly stated in the beginning of the previous and present Office actions. The rejection was not withdrawn because it was improper, but rather because additional rejection over the prior art was applicable to the pending claims. In no way the withdrawal of the rejection by the Notice of the Panel Decision invalidates the rejection of the pending claims under 35 U.S.C. 112, first paragraph, as not being enabled by the specification. The examiner properly rejected the claims under all existing criteria of 35 U.S.C. 112, first paragraph. The Applicants did not provide any convincing evidence demonstrating the enablement of the claimed "molecular manipulator".

Regarding rejection of the pending claims under 35 U.S.C. 112, second paragraph, the examiner did not find anywhere in the prior art the name "line" for defining the probe tip linear extension, which should be a conventional term, according to the specification. The examiner respectfully requests the Applicants to provide any reference, which explains the term "line" in relation to the tip extension, because at present the term is unclear and indefinite and is not explained in the specification in the proper manner. It is not clear, what the "linear extension" of the tip might be.

Regarding the term "moiety located between two arms", with the two arms of the "molecular manipulator" supposedly being able to hold another molecule, it is not apparent, as to why "the moiety located between two arms" should be interpreted as a central part of the same molecule. It is not quite clear, why the "moiety located between two arms" would not be that other molecule that is hold by two arms. It is also not clear, as why the moiety could not be called "a central fragment of the molecule between two arms", which would make the definition much clearer and less ambiguous.

The rejection over the prior art is modified in view of the amendment.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yelena G. Gakh, Ph.D. whose telephone number is (571) 272-1257. The examiner can normally be reached on 9:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill A. Warden can be reached on (571) 272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

12/11/2007

YELENA GAKH
PRIMARY EXAMINER